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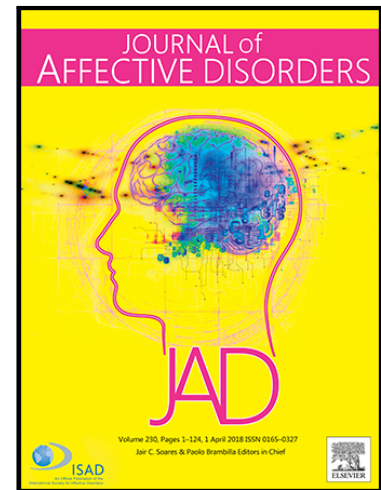
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Highlights

- Handgrip strength and weight status have been independently associated with depressive symptoms in older adults.
- This study investigated the relationship between handgrip strength and depressive symptoms by weight status in older US adults.
- Among older US adults, women and people who are obese and depressed are at the greatest risk of decline in handgrip strength.

Depressive symptoms, handgrip strength, and weight status in US older adults

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ACCEPTED MANUSCRIPT

Abstract

Background: Handgrip strength is a valid indicator of broader physical functioning. Handgrip strength and weight status have been independently associated with depressive symptoms in older adults, but no study has yet investigated the relationships between all three in older US adults. This study investigated the relationship between physical function and depressive symptoms by weight status in older US adults.

Methods: Cross-sectional data were analysed from the National Health and Nutrition Examination Survey waves 2011 to 2012 and 2013 to 2014. Physical function was assessed using a grip strength dynamometer. Depressive symptoms were assessed using the self-reported Patient Health Questionnaire-9. Weight status was assessed using Body Mass Index (BMI) and participants were categorised as normal weight ($<25 \text{ kg/m}^2$), overweight ($25 \text{ to } <30 \text{ kg/m}^2$), and obese ($\geq 30.0 \text{ kg/m}^2$). Associations between depressive symptoms and hand grip strength were estimated by gender-specific multiple linear regressions and BMI stratified multivariable linear regression.

Results: A total of 2,812 adults (54% female, mean age 69.2 years, mean BMI 29.2 kg/m^2) were included. Women with moderate to severe depressive symptoms had 1.60 kg (95% CI: 0.91 to 2.30) lower hand grip strength compared to women with minimal or no depressive symptoms. No such association was observed in men. Among those with obesity, men (-3.72 kg , 95% CI: -7.00 to -0.43) and women (-1.83 kg , 95% CI: -2.87 to -0.78) with moderate to severe depressive symptoms both had lower handgrip strength.

Conclusion: Among older US adults, women and people who are obese and depressed are at the greatest risk of decline in physical function.

Key words: Handgrip strength; physical function; depression; overweight

1. Introduction

Decline in objective physical performance is a common feature of aging in adults (Veronese et al. 2016, Veronese et al. 2017a, Veronese et al. 2017b) and increases the risk of falls, health care use, level of dependency, admissions to residential care, and mortality (Freedman et al., 2002, Gill and Kurland, 2002). United States national statistics indicate that 20% of noninstitutionalized people aged 70 years and older need help in performing at least one activity of daily living (ADL), including bathing, dressing, eating, toileting, and transferring (Kramarow et al., 1999). Indeed, for many independent older adults everyday tasks such as climbing stairs require functioning close to maximal capacity, meaning that further decline could increase their risk of becoming dependent on a carer (Rikli, 1999).

Several studies have shown that handgrip strength is a valid measure of physical function and is a non-invasive measure of physical health that has been widely used in research and clinical settings (Giampaoli et al., 1999, Rantanen et al., 1999, Rantanen et al., 2002, Onder et al., 2005). Taekema et al. (2010) found that dynamometer determined handgrip strength could be a useful instrument in geriatric practice to identify the 'oldest old' patients (i.e. those aged over 75 years) at risk of disability.

Depression is a leading cause of years lived with disability globally (Whiteford et al., 2015) and is associated with decreased physical activity (Vancampfort et al. 2017, Schuch et al. 2017) and objective physical performance (Stuck et al., 1999, Callahan et al., 1998, Dalle Carbonare et al., 2009). However, literature suggests that only older adults with chronic depression, not those with remitted depression are at a greater risk of physical decline than those never depressed (Penninx et al., 2000, Lenze et al., 2005). One study examined the association between different trajectories of depressive symptoms over 1 year and change in functional status over 30 months among patients undergoing coronary angiography; the study concluded that patients with persistent depressive symptoms were at greatest

risk for worse functional status 30 months following coronary interventions (Wilcox et al., 2016). Moreover, a recent meta-analysis (Soysal et al. 2017) found that in participants with depression the prevalence of frailty was 40.4%. In longitudinal studies including older adults with depression at baseline the pooled OR for incident frailty was 3.72 (95% CI 1.95-7.08).

Two previous cross-sectional studies have suggested that handgrip strength is associated with depression (Gale et al., 2011, van Milligen, 2011). Another study using a large population-based adult sample from two Japanese municipalities found that lower hand-grip strength, standardised using age and gender, was both cross-sectionally and longitudinally associated with depressive symptoms (Fukumori et al., 2015). Other more recent studies have found similar results (Veronese et al. 2017b).

The presence of depression, disease and/or disability can lead to a cycle of health decline, particularly in older adults (Kelley-Moore and Ferraro, 2005). One potential consequence of depression is weight gain. In a systematic review, people with depression were found to have an 18% increased risk of being obese (de Wit et al., 2010). A meta-analysis of longitudinal studies found a bi-directional associations between obesity and depression in both men and women, suggesting that the presence of obesity increased the risk of depression – 55% increased risk – and likewise depression was predictive of developing obesity – 58% increased risk (Luppino et al., 2010). More recent systematic reviews have found similar results (Vancampfort et al. 2015). The association between depression and obesity has been shown to be strongest in severely obese persons (Onyike et al., 2003) and the odds ratio for depression increases with BMI, suggesting a dose-response gradient (Dong et al., 2004).

Overweight and obesity have been shown to be associated with depression (Luppino et al., 2010) and decline in physical function (Jensen and Friedmann, 2002 and Roberts et al. 2000) and this literature suggest that this relationship is likely to be bidirectional.

To date no paper has investigated the relationship between handgrip and depression by weight status in older US adults. Research needs to address this gap in the literature to identify whether the overweight/ obese and depressed are at the greatest presence of decline in physical function and thus inform targeted and preventive interventions.

In a large representative cohort of older US adults this paper aims to investigate the association between handgrip strength and depression by weight status. We hypothesise that those who are depressed and overweight or obese will have the lowest levels of grip strength.

2. Methods

2.1. Study Population

The National Health and Nutrition Examination Survey (NHANES) was designed to provide cross-sectional estimates on the prevalence of health, nutrition, and potential risk factors among the non-institutionalized civilian U.S. population up to 85 years of age (Centres for Disease Control and Prevention, 2016). In brief, NHANES surveys a nationally representative complex, stratified, multistage, probability clustered sample of about 5,000 participants each year in 15 counties across the country. Survey participants were asked to attend physical examination in a mobile examination center (MEC). The NHANES obtained approval from the National Center for Health Statistics Research Ethics Review Board and participants provided written consent. We extracted and aggregated data on handgrip strength, depressive symptoms, and other characteristics from NHANES in 2011 to 2012, and 2013 to 2014. We restricted our sample to older adults (≥ 60 years).

2.2. Variables

2.2.1. Handgrip strength (Outcome variable)

The handgrip strength test protocol is detailed in the NHANES Muscle Strength Procedures Manual (Centres for Disease Control and Prevention, 2011). In brief, handgrip strength in kilogram (kg) was measured with the Takei Digital Grip Strength Dynamometer over three trials separately by 60 seconds and alternating hands. A trained examiner explained and demonstrated the protocol to the participant. Participants were asked to squeeze the dynamometer for a practice trial using submaximal effort to determine their understandings on the procedure and the grip size adjustments. They were randomly assigned to start the test with their dominant or non-dominant hand. To complete the test, participants were asked to use one hand to squeeze the dynamometer as hard as possible, and repeated using the other hand for an overall of three alternating hands. Similar to previous studies using this measure, we extracted the maximum value achieved using either hand as the summary measure (Steiber, 2016), studies have retrieved consistent results irrespective of using maximum or average values (Haidar et al., 2004).

2.2.2. Depressive symptoms (Exposure variable)

Depressive symptoms were assessed using the Patient Health Questionnaire (PHQ-9), a valid 9-item depression screener asking about the frequency of symptoms of depression over the past 2 weeks (Kroenke et al., 2001). Each item was scored on a 0-3 scale. The total score of PHQ-9 ranged from 0 to 27, and were categorised as “none or minimum” (0-4), “mild” (5-9), “moderate” (10-14), “moderately severe” (15-19), and “severe” (20-27) for depression severity. For current analyses, participants who scored 10 or more were combined into one group as *clinically relevant* depression. Such diagnosis has

shown a sensitivity of 88 % and a specificity of 88 % for major depression (Manea et al., 2012, Kroenke et al., 2001).

2.2.3. BMI (Exposure variables)

Weight and height were measured at the time of physical examination in the MEC. The measurements followed standard procedures and were carried out by trained technicians using standardized equipment. BMI was calculated as weight in kg/(height in meters)². We categorized study participants into standard BMI categories: underweight (<18.5 kg/m²), normal weight (18.5 to <25 kg/m²), overweight (25 to <30 kg/m²), and obese (≥30.0 kg/m²). Those participants who were underweight were excluded owing to potential underlying physical conditions.

2.2.3.1. Covariates

2.2.3.2. Socio-demographic characteristics and Self-reported leisure-time physical activity (LTPA)

Data on age, sex, race and ethnicity, education and smoking status were extracted. Based on self-reported race and ethnicity, participants were classified into one of the three racial/ethnic groups: Non-Hispanic White, Non-Hispanic Black, and Hispanic and others. Participant's education levels were classified into four groups: less than high school, high school, some college, and college graduate or above. Marital status was summarized into two groups: live with someone (married, and living with partner), and live alone (widowed, divorced, separated, never married). Finally, we classified participants into three smoking groups: never smokers (did not smoke 100 cigarettes in life and do not smoke now), former smokers (smoked 100 cigarettes in life and do not smoke now), and current smokers (smoked 100 cigarettes in life and smoke now). Activity patterns were self-reported by participants using

questions based on the Global Physical Activity Questionnaire (GPAQ) (Hallal et al., 2012). Levels of LTPA were calculated as the minutes per week that participants reported participating in moderate-to-vigorous-intensity physical activity (MVPA). Participants reported the frequency, and duration of physical activity (PA) in a typical week, at vigorous and moderate intensities, respectively. We summarized the total number of minutes for PA in each intensity, where the number of minutes spent in vigorous-intensity PA were doubled and added to the number of minutes of moderate-intensity PA to approximately equivalent the metabolic equivalent of task value (Zhao et al., 2014).

2.2.3.3. Medical Conditions

We included four chronic conditions known to be associated with depression: cardiovascular diseases, diabetes, cancer and arthritis (Vancampfort et al. 2016, Stubbs et al. 2017, Bortolato et al. 2017, Correll et al. 2017). Participants were considered as having chronic illness if they self-reported ever been told by a physician that they have the following conditions: congestive heart failure, coronary heart disease, heart attack, a stroke, diabetes, cancer or arthritis.

2.3. Statistical Analysis

Survey analysis procedures were used to account for the sample weights (MEC exam weight), stratification, and clustering of the complex sampling design to ensure nationally representative estimates. NHANES adults aged 60 years and older with completed information on depressive symptoms, handgrip strength, BMI and other characteristics were included in the analyses. Descriptive characteristics were analysed separately in men and women, due to the documented gender difference in depression (Piccinelli and Wilkinson, 2000) and muscle strength (Perna et al., 2016). We summarized

weighted means and standard errors for continuous variables, weighted proportions for categorical variables, and provided explorative P -values for gender comparison.

Gender-specific multiple linear regressions were carried out to quantify associations between levels of severity in self-reported depression symptoms and handgrip strength. The multivariable models were adjusted for age, race, BMI, education level, smoking status, level of LTPA, and chronic conditions. A cross-product term with BMI, gender and depression symptom severity was entered into the multivariable linear regression with the main effect terms. A statistically significant interaction ($P < 0.001$) was found using the Wald test. We stratified the analyses by BMI categories and estimated the linear associations of depression symptom severity and handgrip strength in each BMI stratum. We examined the normality of residuals using kernel density estimate and standardized normal probability plots for all the linear regression models.

The following sensitivity analyses were conducted: 1) using handgrip strength defined as the maximal value of dominant hands; 2) using handgrip strength defined as the sum of the maximal value of both hands in the multivariable regression models, for men and women, respectively. Stratified models using survey analysis procedure were conducted within subpopulations defined within each strata. All statistical significance was set at $p < 0.05$. All statistical analyses were performed using STATA version 14.0 (STATA Corp., Texas, USA).

3. Results

There were 2,812 adults greater than 60 years of age in the two NHANES waves who had data on handgrip strength and depressive symptoms. Participants' mean age was 69.2 years at the time of examination, and their mean BMI was 29.2 kg/m². We observed significant gender differences in most

characteristics, except for age and race (Table 1). There were more men than women with BMI ≥ 25.0 kg/m², had a college graduate degree or above, lived with someone, were a former or current smoker, did not have chronic conditions, were sufficiently physically active; had higher handgrip strength, and had minimal or no depressive symptoms.

In the gender-specific models, women with moderate to severe depressive symptoms had 1.60 kg (95% CI: 0.91 to 2.30) lower handgrip strength comparing to those with none or minimum depressive symptoms adjusted for age, BMI, race and ethnicity, education, marital status, smoking status, level of leisure-time physical activity, and chronic conditions (cardiovascular disease, diabetes, cancer and arthritis). No such association was observed in men.

Table 2 summarizes analyses stratified by BMI categories, for men and women respectively. We observed an interaction ($P < 0.001$), such that the associations of depressive symptom severity with handgrip strength differed within each BMI and gender stratum. Among older adults with normal weight BMI, there were no associations between depressive symptoms severity and handgrip strength in men (-1.25 kg, 95% CI: -4.64 to 2.15 in mild depressive symptoms severity, 1.45 kg, 95% CI: -5.64 to 8.54 in moderate to severe depressive symptoms severity) or women (0.22 kg, 95% CI: -0.92 to 1.35 in mild depressive symptoms severity, -1.10, 95% CI: -2.97 to 0.60 in moderate to severe depressive symptoms severity). Overweight men with mild depressive symptoms had lower handgrip strength (-4.12 kg, 95% CI: -6.25 to -1.99), but not those with moderate to severe depressive symptoms (2.01 kg, 95% CI: -0.51 to 4.52), nor overweight women (0.86 kg, 95% CI: -0.28 to 1.20 in mild depressive symptoms severity, -0.93 kg, 95% CI: -2.91 to 1.05 in moderate to severe depressive symptoms severity). Among those with obesity, men (-3.72 kg, 95% CI: -7.00 to -0.43) and women (-1.83 kg, 95% CI: -2.87 to -0.78) with moderate to severe depressive symptoms both had lower handgrip strength.

Our findings were similar when using handgrip strength defined as the maximal value of dominant hands or as the sum of the maximal value of both hands. Women with moderate to severe depressive symptoms had lower maximal value of dominant handgrip strength (-1.71 kg, 95% CI: -2.47 to -0.95), and lower sum of maximal value of both handgrip strength (-3.01 kg, 95% CI: -4.52 to -1.51). These associations were found in both men and women with obesity (Data not shown).

4. Discussion

To our knowledge, this is the first study to investigate the association between handgrip strength and depression by weight status in older US adults. We found in a large representative sample of older US adults that, among females only, those who were categorised as having moderate to severe depression had significantly lower dynamometer determined handgrip scores than those who were categorised as having no depression. The lack of association in men is interesting, though the mechanism underlying this gender difference is unclear. One possible explanation may be that severity of depressive symptoms is greater in women than men (Albert, 2015, de Wit et al., 2010). Indeed, in this sample more women than men suffered from severe depression. Depression is more than twice as prevalent in young women than men (ages 14–25 years old), and this ratio decreases with age (Albert, 2015). It is possible that prolonged exposure to depression and its symptoms across the lifespan contributes to a greater decline in physical function in adulthood. Further research is required to test this hypothesis. Another explanation may be related to fluctuations in ovarian hormones through the lifespan, particularly oestrogen. During the perimenopausal transition, there appears to be an increased risk of depression (Cohen et al., 2006), however the use of hormone replacement therapies during this time have been shown to effectively prevent postmenopausal depression in women (Gordon and

Girdler, 2014). Hormonal fluctuations may therefore be a potential trigger for depression in women (Albert, 2015), which may lead to decline in physical function.

We observed lower handgrip strength in those with severe depression, which supports findings from previous cross-sectional work. A growing body of literature shows weaker hand grip strength to be associated with a lower physical quality of life (Giampaoli et al., 1999, Rantanen et al., 2002, Rantanen et al., 1999) low physical quality of life in turn is likely to have a detrimental impact on mental health and thus depression (Callahan et al., 1998, Whiteford et al., 2015). On the other hand, those with depressive symptoms might be likely to develop weaker hand-grip strength, in so far as depression might cause decline in systemic physical functioning (Penninx et al., 1999). For instance, depressive symptoms – such as changes in appetite, smoking and/or drinking alcohol, sleep disturbances and reductions in physical activity – have the potential to change body composition and metabolism, in turn influencing noncommunicable disease risk, and so promoting declines in physical functioning (Lenze et al., 2001). Indeed, older adults who received an effective treatment for depression, including educational materials and consultations with depression clinical specialists, showed improvements and better preservation of physical functioning than older adults receiving usual care at 3, 6 and 12 month follow-up assessments (Callahan et al., 2005).

In the present study, when data were stratified by weight status we found that both men and women who were obese and had moderate to severe depression had significantly lower hand grip scores compared to those who were obese and had no depression. Obese people can plausibly engage in an active lifestyle even at a light intensity. However, a person who is both obese and depressed may not do so, as both obesity and depression are associated with lower levels of physical activity, instead leading a sedentary lifestyle which may result in greater decline in physical function (Schuch et al. 2017;

Stubbs 2018). This may potentially result in sarcopenia, a syndrome characterised by progressive and generalized loss of skeletal muscle mass and strength with a risk of adverse outcomes such as physical functional decline, poor quality of life and death (Cruz-Jentoft et al. 2010).

To the authors knowledge this is the first paper to investigate the association between physical functioning, measured using handgrip strength, and depression by weight status in older US adults. A clear strength of this study is the large representative sample of older US adults. There are a number of limitations to this study. First, the cross-sectional nature of this study makes it impossible to determine a causal association. That is, it is not known whether obesity and depression cause decline in physical function or whether a decline in physical function results in obesity and depression. Further research using either a longitudinal or experimental design is warranted.

The present study suggests that women and those who are obese and depressed are at the greatest risk of decline in physical functioning. Interventions designed to prevent a decline in physical functioning in these populations may be bettered by utilizing not only physical aspects but mental health strategies to improve and sustain health in older adults for independent living.

Conflicts of Interest

None declared

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Table 1. Socio-demographic Characteristics of Adults Aged 60 Years or Older from the NHANES (2011-2014), by Gender

		Men	Women	<i>P</i> -values
	<i>N</i>	1380	1432	
	Weighted <i>N</i>	23,433,910	27,597,944	
Age (years)	Mean (s.e.)	68.9 (0.3)	69.5 (0.3)	0.085
BMI (kg/m ²) (continuous)	Mean (s.e.)	29.0 (0.3)	29.4 (0.3)	0.203
BMI (kg/m ²)				0.002
18.5 – 24.9	n (%)	22.7	27.9	
25.0 – 29.9	n (%)	41.4	31.9	
≥ 30	n (%)	35.9	40.2	
Race				0.222
Non-Hispanic White	n (%)	80.2	78.4	
Non-Hispanic Black	n (%)	7.6	9.1	
Hispanic and Other	n (%)	12.2	12.5	
Education				<.001
Less than 12th grade	n (%)	16.4	17.3	
High School	n (%)	19.1	23.9	
Some college	n (%)	28.3	34.0	
College graduate or above	n (%)	36.2	24.8	
Marital status				<.001
Live with someone	n (%)	78.6	53.2	
Live alone	n (%)	21.4	46.8	
Smoking				<.001
Never smoker	n (%)	39.4	58.8	
Former smoker	n (%)	48.6	31.9	
Current smoker	n (%)	12.0	9.3	
Chronic conditions				0.033
Yes	n (%)	66.5	71.6	
No	n (%)	33.5	28.4	

Leisure time physical activity (LTPA)				0.010
Inactive	n (%)	52.3	56.1	
Insufficiently Active	n (%)	14.5	16.7	
Sufficiently Active	n (%)	33.2	27.2	
Handgrip strength defined sarcopenia	n (%)	9.6	15.3	<.001
Handgrip strength (continuous)	Mean (s.e.)	39.8 (0.4)	24.7(0.2)	<.001
Depressive symptoms				<.001
None or minimum	n (%)	84.1	74.4	
Mild	n (%)	10.5	17.2	
Clinically relevant	n (%)	5.4	8.4	

Table 2. Associations between Depressive Symptoms and Handgrip Strength by Weight Status from Multiple Linear Regression Models among Adults Age 60 Years and Older from the NHANES (2011-2014).				
	Unadjusted Beta-coefficient (95% CI)	Adjusted ^a Beta-coefficient (95% CI)	Unadjusted Beta-coefficient (95% CI)	Adjusted ^a Beta-coefficient (95% CI)
Normal weight				
	Men (n=357)		Women (n=371)	
None or minimum (0-4)	Reference	Reference	Reference	Reference
Mild (5-9)	-3.64 (-7.32 to 0.05)	-1.25 (-4.64 to 2.15)	-0.47 (-1.66 to 0.72)	0.22 (-0.92 to 1.35)
Moderate to severe (10-27)	-1.78 (-8.28 to 4.73)	1.45 (-5.64 to 8.54)	-0.69 (-3.02 to 1.64)	-1.10 (-2.97 to 0.60)
Overweight				
	Men (n=567)		Women (n=437)	
None or minimum (0-4)	Reference	Reference	Reference	Reference
Mild (5-9)	-5.30 (-7.34 to -3.26)	-4.12 (-6.25 to -1.99)	0.13 (-1.36 to 1.62)	0.86 (-0.28 to 1.20)
Moderate to severe (10-27)	2.65 (-0.42 to 5.72)	2.01 (-0.51 to 4.52)	-1.33 (-3.13 to 0.48)	-0.93 (-2.91 to 1.05)

Obese				
	Men (n=456)		Women (n=624)	
None or minimum (0–4)	Reference	Reference	Reference	Reference
Mild (5–9)	-0.58 (-3.25 to 2.10)	0.34 (-2.18 to 2.87)	-0.12 (-1.51 to 1.26)	0.31 (-0.94 to 1.57)
Moderate to severe (10–27)	-4.36 (-7.47 to -1.25)	-3.72 (-7.00 to -0.43)	-1.91 (-3.07 to -0.76)	-1.83 (-2.87 to -0.78)
^a Adjusted for age, race and ethnicity, education, marital status, smoking status, level of leisure-time physical activity, and chronic conditions (cardiovascular diseases, diabetes, cancer and arthritis).				

